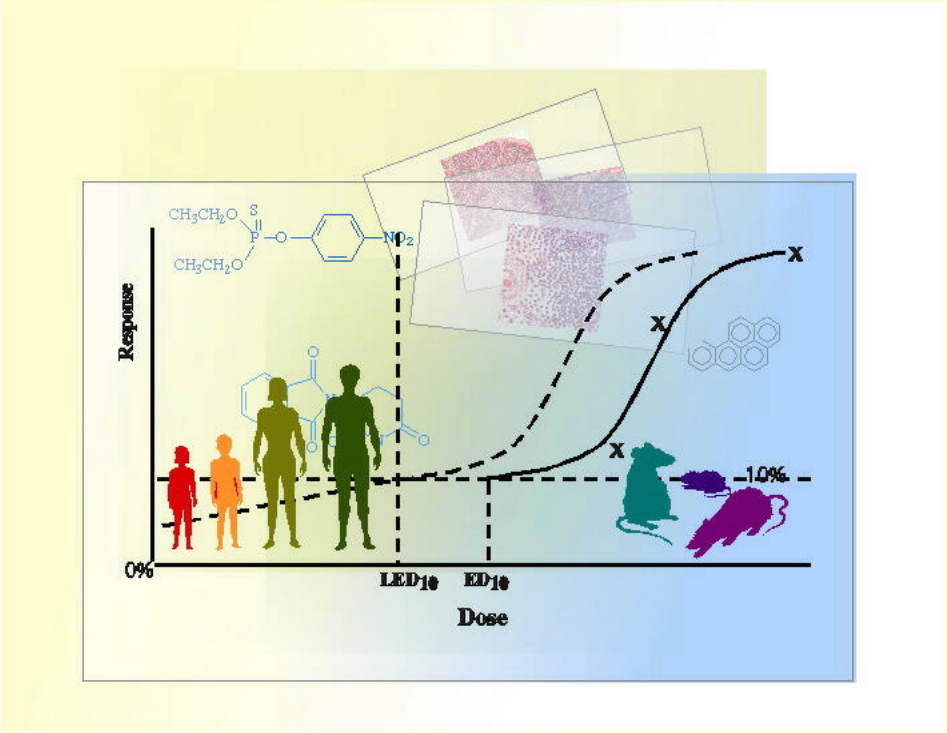
HUMAN HEALTH RISK ASSESSMENT

Sulfotepp



U.S. Environmental Protection Agency
Office of Pesticide Programs
Health Effects Division (7509C)

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HUMAN HEALTH RISK ASSESSMENT *for*

Sulfotepp

Phase IV

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I. Executive Summary

The following assessment evaluates risks from inhalation and dermal exposure from both handling Sulfotepp and reentering areas treated with Sulfotepp. This assessment also considers short-term and intermediate-term exposures.

The inhalation risk assessment is based on an endpoint and dose obtained from a route-specific study obtained from a secondary data source. This study was cited by American Conference of Governmental industrial Hygienists (ACGIH) as the data source for setting the threshold limit value (TLV)/permissible exposure limit (PEL).

The intermediate-term dermal risk assessment is based on an endpoint and dose established in a non-route-specific (oral) subchronic toxicity study, classified as acceptable by the Agency for regulatory purposes. However, the dose used for short-term dermal risk assessment is an extrapolation based on the results seen in similar organophosphate pesticides.

Application and postapplication inhalation exposure data are taken from a secondary data source and postapplication dermal exposure estimates are based on a Cal EPA residue study which is not GLP/guideline acceptable.

Due to the significant lack of data, Sulfotepp has not been reviewed by the Agency's Health Effects Division (HED) Hazard Identification Committee. This Committee evaluates toxicological data for adequacy, establishes endpoints and doses for risk assessment, and most significantly for Sulfotepp, establishes Margin-of-Exposure (MOE) requirements for risk assessment and regulatory purposes. Although data gaps as seen in the Sulfotepp database typically increase MOE requirements to significantly higher levels than the standard 100 used to account for inter- and intra-species variability, this assessment will refer to 100 as an assumed minimum.

For these reasons, the following revised risk assessment is likely to change based on new data and discussions with the registrants (and growers) which the Agency considers essential for the resolution of all the outstanding issues and concerns.

Based on the use patterns, two pesticide handler scenarios were identified: (1) opening and lighting of canisters; and (2) reentering fumigated greenhouses to open vents and dispose of canisters. For handlers, dermal exposures are assumed to be small, infrequent and of short duration relative to exposures from inhalation. Potential dermal exposure is limited to possible contact with the Sulfotepp formulated product while opening the canisters and inserting the sparkler, an accidental spill, and possible contact with residue on the outside of a spent canister. These dermal exposures are expected to be relatively infrequent and of relatively short duration in comparison with the estimated inhalation exposure and the potentially high air concentrations of Sulfotepp during handling activities. Therefore, only inhalation exposures and risks were estimated for handlers. For handler inhalation risk, the Agency has determined a range of MOEs varying from 32,000 for a one-hour exposure for self-contained breathing apparatus to two for a one-hour exposure under the current label, which requires the use of a half-face respirator. When using a self-contained breathing apparatus, the MOEs do not represent a risk of concern.

Two postapplication scenarios were identified: (1) entry to perform watering or other routine low exposure tasks; and (2) entry to perform harvesting, transferring, or other high exposure tasks. For postapplication exposure, both dermal and inhalation exposures were assessed. Short and intermediate term risks were calculated. Results indicate for total risk (combined dermal plus inhalation) that short-term MOEs range from one to 14, and intermediate-term MOEs range from 0.3 to seven (at all air concentration levels for both low and high exposure activities up to 38 hours following fumigation). Current labeling allows reentry between two and 24 hours after fumigation, depending on how the greenhouse is ventilated. These MOEs represent a concern for all postapplication scenarios.

II. Human Health Risk Assessment

A. Hazard Identification

1. Acute Toxicology Categories

The toxicological database for Sulfotepp (0,0,0,0-tetraethyl-dithio-diphosphate) is incomplete. The Sulfotepp label indicates that it is classified as restricted-use due to very high toxicity to humans.

2. Other Endpoints of Concern

No route-specific data were available to obtain a short- or intermediate-term NOEL for dermal exposures. No route-specific Agency-reviewed data were available to obtain a NOEL for inhalation exposures.

a. Intermediate-Term Dermal Endpoint

Since an acceptable route-specific study is not available to assess Sulfotepp dermal exposure and risk, HED is basing the following *dermal* risk assessment on the results of the subchronic feeding study in dogs (MRID 42955601) that has been reviewed and graded as *acceptable* by the Agency (U.S. EPA, 1995).

In the study, male and female beagle dogs were given E393 (Sulfotepp) in the diet at concentrations of 0, 0.014, 0.11, 0.55, or 2.75 mg/kg/day in males, and 0.014, 0.12, 0.57, or 3.07 mg/kg/day in females. No treatment-related effects were observed for food consumption, body weight gain, hematology, gross or microscopic pathology, or most clinical chemistry parameters. Occasional diarrhea and vomiting were seen in dogs receiving 0.55/0.57 mg/kg/day and these signs were common in dogs given 2.75/3.07 mg/kg/day. Mean cholinesterase activities in erythrocytes and plasma were statistically ($p < 0.05$) reduced in high dose males and females as compared to controls throughout the entire study. There was also a dose-responsive decrease in plasma cholinesterase activity beginning with the 0.11 mg/kg/day male group and the 0.014 mg/kg/day female group. No differences were seen at necropsy in brain cholinesterase activity of any treated group as compared to controls.

Under the conditions of this study, the LOEL for clinical signs of toxicity from dietary exposure to E393 is 0.55 mg/kg/day and the NOEL is 0.11 mg/kg/day. Based on the dose responsive inhibition of 10% or greater of plasma cholinesterase activity, the LOELs for male and female Beagle dogs are 0.11 mg/kg/day, and the NOEL for males is 0.014 mg/kg/day. The NOEL of 0.014 mg ai/kg/day is used in the risk assessment for evaluating *intermediate-term* dermal risks to postapplication workers. A NOEL for female cholinesterase activity was not identified.

b. Short-Term Dermal Endpoint

To estimate a surrogate *short-term* NOEL for Sulfotepp, EPA referred to data for ethyl parathion, another organophosphate pesticide that is believed to be similar in nature to Sulfotepp. The intermediate-term NOEL for ethyl parathion is 0.0024 mg/kg/day based on a 180-day oral toxicity study in dogs that showed reduced cholinesterase activity by week six (U.S. EPA, 1998b). The short-term NOEL for ethyl parathion is 0.025 mg/kg/day based on an oral acute neurotoxicity study on rats in which plasma and RBC cholinesterase inhibition was observed. The short-term NOEL is, therefore, approximately 10 times higher than the intermediate-term NOEL for ethyl parathion. Assuming that the ratio of short-term to intermediate-term NOEL would be the same for Sulfotepp as it is for ethyl parathion, the short-term NOEL for Sulfotepp was estimated to be 0.14 mg ai/kg/day. This value was used in the risk assessment for evaluating short-term dermal risks to postapplication workers.

c. Dermal Absorption

The NOELs for the dermal short- and intermediate-term risk assessments are based on an oral study. EPA notes that the Occupational Safety and Health Agency's (OSHA) Sulfotepp PEL has a *skin notation* because data indicate that Sulfotepp penetrates the skin in amounts sufficient to induce systemic toxicity (American Conference, 1995). The National Institute for Occupational Safety and Health (NIOSH) concurs with the OSHA PEL with *skin notation* for Sulfotepp (American Conference, 1995). In addition, the ACGIH has established a TLV for Sulfotepp and also placed a *skin notation* on the value (American Conference, 1995). Therefore, in lieu of dermal absorption data and in light of the *skin notation* on the PEL/TLV, EPA is assuming 100 percent dermal absorption.

d. Inhalation Endpoint

The ACGIH has established a TLV based on the results of a Sulfotepp subchronic inhalation study published in 1974 (American Conference, 1995; Kimmerle, *et.al*., 1974). Although this study has not been reviewed by the Agency, the endpoint and dose (NOEL) reported in this study are the basis for the following *inhalation* risk assessment.

For 12 weeks, four groups of 10 male and 10 female rats were exposed to different aerosol concentrations of Sulfotepp for six hours daily, five days per week. The concentrations were 0, 0.89, 1.94, and

2.83 mg/m^3 and cholinesterase in plasma and erythrocytes was determined at week 1, 4, 6, 8, and 12. Laboratory examinations were also performed at week 12. Sulfotepp concentrations were measured by gas chromatograph. The exposure to Sulfotepp aerosol at up to 2.83 mg/m^3 did not cause any significant changes in appearance, behavior, or body weight gain. The hematological values and serum-enzyme activities as well as serum concentrations of urea, creatinine, protein, and bilirubin were not altered and there was no significant change in the composition of the urine. The Sulfotepp concentrations of 0.89 and 1.94 mg/m^3 (study NOEL) caused no depression of cholinesterase activity in plasma and erythrocytes and at 2.83 mg/m^3 (LOEL) caused significant inhibition of plasma cholinesterase activity. On the basis of this study, EPA established an inhalation NOEL of 1.94 mg/m^3 for Sulfotepp.

e. Chronic-Term Endpoints

Given the nature of Sulfotepp use patterns, no chronic exposures are anticipated.

f. Cancer Endpoint

Carcinogenicity studies have not been required or reviewed by the Agency.

g. PEL/TLV

OSHA has established a PEL as a time-weighted average of 0.2 mg/m^3 for Sulfotepp (American Conference, 1995). NIOSH concurs with the OSHA PEL (American Conference, 1995). In addition, the ACGIH has established a TLV as a time-weighted average of 0.2 mg/m^3 for Sulfotepp (American Conference, 1995). The OSHA, NIOSH, and ACGIH inhalation limits are based on the subchronic inhalation study discussed above. Also, NIOSH has established a value of 35 mg/m^3 for Sulfotepp as a level that is “immediately dangerous to life or health” (IDLH) (American Conference, 1995).

h. Margin-of-Exposure

An MOE of 100 or greater is generally considered adequate by the Agency for both the short- and intermediate-term dermal and inhalation risk assessments. This includes a 10-fold safety factor for interspecies variability and a 10-fold safety factor for intraspecies variability. Due to the lack of acceptable data for Sulfotepp, HED has not determined a MOE

that is considered adequate (although it can be assumed that 100 is the minimum requirement).

3. Data History

On September 30, 1988, the Agency issued a Registration Standard for the active ingredient Sulfotepp. The standard required that registrants submit the following generic toxicological data for the technical grade of the active ingredient:

- Acute Oral Toxicity - Rat (Guideline 81-1)
- Acute Dermal Toxicity - Rabbit (Guideline 81-2)
- Acute Inhalation Toxicity - Rat (Guideline 81-3)
- Eye Irritation - Rabbit (Guideline 81-4)
- Dermal Irritation - Rabbit (Guideline 81-5)
- Dermal Sensitization - Guinea Pig (Guideline 81-6)
- Acute Delayed Neurotoxicity - Hen (Guideline 81-7)

- 21-Day Dermal - Rabbit (Guideline 82-2)
- 90-Day Inhalation - Rat (Guideline 82-4)
  (**Note:** *HED currently believes that a 21-day inhalation study might be more appropriate.)*

- Teratology - one species (Guideline 83-3)
- Mutagenicity Studies (Guideline 84-2)

- *Reserved:* 90-Day Dermal - Rat (Guideline 82-3)
- *Reserved:* Pending Results of Guideline 81-7 -- 90-Day Neurotoxicity (Guideline 82-5)

In addition, in 1991, the Agency issued a data call-in (DCI) for Sulfotepp neurotoxicity data (Guidelines 81-8-SS, 82-5(b), and 85-7-SS).

The registrants (Fuller System, Inc. and Plant Products Corporation) committed to provide the required data and to this end submitted studies purchased from the technical supplier (Bayer).

In the interim, the Agency has received and completed the review (U.S. EPA, 1995) of three studies submitted collectively in response to the DCI. The three studies are: (1) a subchronic feeding study in the dog (82-1b); (2) an acute oral toxicity in the hen; and (3) an NTE/cholinesterase study in the hen. The subchronic dog study was classified as “Core Minimum” and is considered acceptable for regulatory purposes. The hen studies were classified as “Core

Supplementary" and may be used in support of an acute delayed neurotoxicity study but the studies are not considered acceptable for regulatory purposes.

Sulfotepp toxicology data have been screened by HED and the status of the data set is summarized in the following table (Table 1). The toxicology endpoints and NOAELs for new studies which have been submitted to the Agency but have not been completely reviewed (currently in secondary review) will not change the short- and intermediate-term endpoints and doses that are the basis of this risk assessment.

Table 1. Toxicology Profile

Guideline	Study Type/Report No./MRID No.	Comments
Acceptable Guideline Studies		
82-1(b)	90-Day Feeding - Dog Bayer Study No 5756 1 Dec 1975 MRID 43615401	Study submitted and reviewed and found to be ACCEPTABLE (GUIDELINE).
Unacceptable Guideline Studies		
81-7	Acute Delayed Neurotoxicity Study - Hen Bayer Study No. T9040988 26 June 1992 MRID 42955602	Study reviewed (HED No. 011602) and found to be UNACCEPTABLE (GUIDELINE)
Studies Submitted (Primary Review Indicates Study Is Acceptable)		
81-6	Dermal Sensitization - Guinea Pig Bayer ID No. T2030144 10 Aug 1989 MRID 41796601 (Duplicate 43606905)	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (GUIDELINE). The study review is currently in secondary review.

Guideline	Study Type/Report No./MRID No.	Comments
83-3(a)	Developmental - Rat Miles Report No. MTD0203 22 Mar 1991 MRID 43401601 (Duplicate 43606906) Miles Report No. MTD0296 3 June 1993 MRID 43606907	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (GUIDELINE). The study review is currently in secondary review. Supplementary data submission to further define the NOAEL. This study is ACCEPTABLE (NON-GUIDELINE).
84-4	Gene Mutation - Ames Bayer, ID No. 17982 & T5030110 27 Apr 1989 MRID 43449103 (Duplicate 43606913)	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (GUIDELINE). The study review is currently in secondary review.
	Gene Mutation - Ames Oesch 4 Nov 1977 MRID 43449104 (Duplicate 43550609)	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (GUIDELINE). The study review is currently in secondary review.
	Test on *S. cerevisiae* D7 Bayer, ID No. 18526, T1030143 14 Nov 1989 MRID 43542702 (Duplicate 43606914)	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (GUIDELINE). The study review is currently in secondary review.
	Dominant lethal test Bayer, ID No. 8286 & E393/004 5 Apr 1979 MRID 43449106 (Duplicate 43606912)	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (GUIDELINE). The study review is currently in secondary review.

Guideline	Study Type/Report No./MRID No.	Comments
	Micronucleus test on the mouse Bayer, ID No. 7917 & E393/003 9 Nov 1978 MRID 43449105 (Duplicate 43606911)	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (GUIDELINE). The study review is currently in secondary review.
	In vitro cytogenetics study with human lymphocytes for the detection of induced clastogenic effects Bayer, Report No. T2032548 9 Mar 1990 MRID 43542703 (Duplicate 43606910)	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (GUIDELINE). The study review is currently in secondary review.
Special Study	Embryotoxicity and Teratogenic Effects in Rats Bayer, Report No. 9171 20 May 1980 MRID 43606908	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (NON-GUIDELINE). The Data Evaluation Record is currently in secondary review.
Special Study	Embryotoxicity Study in Rabbits Bayer, Report No. 12906 4 Sep 1984 MRID 43606909	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (NON-GUIDELINE). The Data Evaluation Record is currently in secondary review.
Special Study	Cholinesterase Activity in F0 and Newborn F1 Rats Albany Medical College Report No. None, 19 May 1976 43550607	This study has been submitted to the Agency. After initial review, it was found to be ACCEPTABLE (NON-GUIDELINE). The Data Evaluation Record is currently in secondary review.

Guideline	Study Type/Report No./MRID No.	Comments
Studies - Primary Review or Not Available for Review		
81-1	Acute Oral - Rat	No study available for review. Data summarized in MRID 43550608, 43356701 and 43550602
81-2	Acute Dermal - Rat	No study available for review. Data summarized in MRID 43550608, 43356701 and 43550602
81-3	Acute Inhalation - Rat	No study available for review. Data summarized in MRID 43356701 and 43550602
81-4	Primary Eye Irritation - Rabbit	No study available for review. Data summarized in MRID 43356701 and 43550602
81-5	Primary Dermal Irritation - Rabbit	No study available for review. Data summarized in MRID 43356701 and 43550602
81-8	Acute Neurotoxicity - Rat	No study available for review; data gap.
82-1(a)	90-Day Feeding - Rat Klimmerle (1968) Bayer Study 29 Oct 1968	No study available for review. Abstract of study presented in MRID 43550602 (Bayer report dated June 1993)
82-2	21-Day Dermal - Rabbit	No study available.
82-4	90-Day Inhalation Study MRID 43606906, 43606915 43356701	No study available for review. Data summarized in MRID 43356701 This study is the basis for the OSHA PEL (0.2 mg/m3) and the ACGIH TLV.
82-5(a)	Subchronic Neurotoxicity Study - Hen	No study available for review.
82-5(b)	Subchronic Neurotoxicity Study - Rat	No study available for review; data gap.
83-1/2	Chronic Feeding/Oncogenicity - Rat Bayer Report No 11640 21 Mar 1983	No study available for review. Abstract of study presented in MRID 43550602 (Bayer report dated June 1993)
83-1(b)	Chronic Feeding - Dog	No study available; data gap.
83-2(b)	Oncogenicity - Mouse	No study available for review. Abstract of study presented in MRID 43550602 (Bayer report dated June 1993)

Guideline	Study Type/Report No./MRID No.	Comments
83-3(b)	Developmental - Rabbit	No study available for review.
83-4	Reproduction, 2 Generation in Rats Bayer Report No 20878 4 Dec 1991	No study available for review. Abstract of study presented in MRID 43550602 (Bayer report dated June 1993)
85-1	General Metabolism	No study available for review. Abstract of study presented in MRID 43550602 (Bayer report dated June 1993)

B. Calculating Risks

1. Dermal Risks

Dermal risk was estimated by dividing the dermal endpoint (NOEL) by the estimated daily dermal dose[1].

2. Inhalation Risks

Inhalation risk was estimated by calculating a route-specific MOE (U.S. EPA, 1998c). The route-specific MOE is preferred over a route-to-route MOE, because there is no need to estimate the percentage of absorption or adjust for metabolism or any other pharmacokinetic parameters. The Science Advisory Panel (SAP) and HED Exposure Science Advisory Committee (SAC) have endorsed the use of route-specific MOEs whenever possible because they are more accurate and are easy to combine with MOEs from other routes of exposure -- even when they have dissimilar uncertainty factors (U.S. EPA, 1998c).

[1]**NOTE**: This document uses the terminology "NOELs" and "LOELs" instead of the terms "NOAELs" and "LOAELs," as is our current policy. The NOELs and LOELs contained in this document and supporting documentation do reflect adverse effect levels, as has always been OPP's policy.

A route-specific MOE is calculated by dividing a NOEL for a route of specific exposure (e.g., inhalation) that is derived from an animal study by the estimated human exposure for the same route of exposure. Since the units are the same (e.g., mg/m^3 for inhalation), they cancel out to yield a unitless MOE. Precision is enhanced by accounting for differences in:

- **D_A** Duration of daily exposure for test animals (hours/day)
- **D_H** Duration of daily exposure for humans (hours/day)
- **AF_A** Activity factor for test animals (default value of one is assigned)
- **AF_H** Activity factor for humans (accounts for activity-related variations in respiration)

The activity factor accounts for increased exposure (e.g., respiratory rate) due to increased activity. The activity factor for the test animals is assigned a default value of one, since animals in a test chamber are assumed to have low activity levels. The activity factor for humans is a ratio of the estimated human respiratory rate while performing certain activities to the estimated human respiratory rate at rest. The activity-specific human respiratory rates are listed in the EPA's "Exposure Factors Handbook" published in 1997 (U.S. EPA, 1997b).

A route-specific inhalation MOE is calculated as follows:

$$MOE = \frac{NOEL(mg / m3) * D_A * AF_A}{Human\ Airborne\ Concentration\ (mg / m3) * D_H * AF_H}$$

C. Epidemiological Information

Four databases have been consulted for the poisoning incident data on the active ingredient Sulfotepp (U.S. EPA, 1998a).

1. OPP Incident Data System (IDS)

The Incident Data System (IDS) indicates two Sulfotepp-related incidents:

- An individual entered two locked greenhouses to which she had a key. Both greenhouses had been treated with Sulfotepp earlier that day but neither greenhouse was posted. After about 10 minutes she experienced nausea, difficulty breathing, and burning lips and eyes. She was

seen in a local emergency room. No further information on the disposition of this case is available.

- In 1995 an applicator to a Texas greenhouse was exposed to Sulfotepp and developed headache, nausea, diarrhea, vomiting, cough, dizziness, sweating, fatigue, abdominal pain, anxiety, muscle aches, chest tightness, drowsiness, restlessness, shortness of breath, and excessive salivation. Blood cholinesterase levels taken 12 hours after the exposure were within the normal range. The applicator reported wearing the required protective equipment including full body suit and full face respirator. His respirator had been fit tested earlier that month and no leaking was detected. However, the worker did report being able to smell the compound. When questioned, two of the other three applicators in the same greenhouse reported that they also smelled the chemical and felt nauseated.

  A subsequent investigation by the State Health department determined that the PPE used was appropriate and in good working order and that all product label directions had been followed. During their on-site investigation the four workers again applied Sulfotepp and three of the four smelled the chemical and the same worker again developed symptoms though less severe.

  A survey of 43 companies that use Sulfotepp in greenhouse applications identified three companies that reported workers who had become ill though none sought medical attention.

  As a result of this investigation the Texas Department of Health recommended appropriate supplied air respirators and training in proper use of fumigants as part of the licensure requirements for greenhouse pesticide applicators. Other procedures recommended involved reducing exposure by pre-punching canisters so that all of them could be ignited at once with minimal time spent with workers carrying ignited canisters or spending unnecessary time in the greenhouse while the smoke is being produced (Morbidity and Mortality, 1996).

2. Poison Control Centers

There were a total of 40 Sulfotepp cases in the Poison Control Centers (PCC's) database. Of these, 23 cases were occupational exposure; 22 (96%) involved exposure to Sulfotepp alone and one (4%) involved exposure to multiple chemicals, including Sulfotepp. There were a total of 14 adult non-occupational exposures; all of which involved this chemical alone. (Workers who were indirectly exposed (not handlers) were classified as non-occupational cases.) Three cases were reported in children under the age of six years (no details are available). Out of 37 reported cases involving adults, there were no life-threatening cases and symptoms were less commonly reported than for other cholinesterase inhibitors.

3. California Department of Food and Agriculture

There were 17 cases involving Sulfotepp submitted to the California Pesticide Illness Surveillance Program from 1982 to 1995. In 16 of these cases, Sulfotepp was used alone and was judged to be responsible for the health effects. None of the individuals were reported hospitalized between 1982 and 1995 and two individuals were reported off work for one day. All 16 persons had systemic illnesses. Three cases occurred in 1984 when Sulfotepp leaked to a work site outside the greenhouse. These cases appear to represent a cluster episode at one work site. Another eight cases occurred in 1995 when material leaked from cracks in the greenhouse. The fumes drifted 200 to 300 feet to a residential area resulting in a cluster of eight poisonings. Exposure to residue was reported in three cases: one involving a worker who returned two hours after treatment and did have on some protective clothing; a second who returned to a greenhouse after 15 hours and after the greenhouse had been ventilated only one hour; and a third case was a truck driver loading plants and possibly exposed to residual vapors at an unknown time after application.

4. National Pesticide Telecommunications Network (NPTN)

On the list of the top 200 chemicals for which NPTN received calls from 1984-1991 inclusively, Sulfotepp ranked 197th and was reported to be involved in eleven human incidents.

5. Summary and Conclusions

Relatively small numbers of reports of illness from Sulfotepp have been identified. Two incidents have been reported to the IDS (1992-1998); 40 incidents to the nation's PCC's (1985-1992); 17 incidents to the California Pesticide Illness Surveillance Program (1982-1995); and 11 incidents to the National Pesticide Telecommunications Network (1984-1991). The California reports suggest that drift outside of improperly sealed greenhouses can pose a hazard to persons nearby. Exposure to residue when reentering has also led to development of symptoms. The most controversial case is the Texas report of poisoning in applicators using proper protective equipment and following proper precautions. In one instance workers reported smelling the product and one developed symptoms while health investigators were on site observing the application. One of the registrants questions whether the symptoms were due to Sulfotepp or due solely to smoke inhalation. A survey in Texas of 43 establishments determined that three (7%) had workers who reported experiencing illness associated with their use of Sulfotepp.

D. Use and Usage

1. Occupational Use Products

a. Type of Pesticides and Target Pests

Sulfotepp is an organophosphate insecticide used for control of certain ornamental pests such as insects, mites, and thrips.

b. Formulation Types and Percent Active Ingredient

Sulfotepp is formulated as impregnated material in smoke generators (canisters) containing 14 to15 percent active ingredient (U.S. EPA, 1997c).

c. Registered Use Sites

Sulfotepp is a restricted-use pesticide used in greenhouses only (EPA Reg. No. 8241-10; 1322-38).

d. Application Rates

The application rate is 0.0033 pound of active ingredient per 1,000 cubic feet (Plantfume 103™; EPA Reg. No. 8241-10).

e. Methods and Types of Equipment Used

The Sulfotepp smoke generators are placed in the greenhouse and then ignited using inserted sparklers to generate a dense white smoke for fumigation.

f. Timing and Frequency of Applications

Fumigation with Sulfotepp may be repeated every three days until the greenhouse is pest free.

g. Additional Notes on Current Use

Sulfotepp is used primarily just before marketing of the plants as a final cleanup of pests to ensure the pest-free status of plants. It is effective against the three most important greenhouse arthropod pests: aphids, spider mites, and whiteflies. The primary use for Sulfotepp in states such as California, Michigan, New York, Ohio, Pennsylvania, and Texas is for whitefly control in mature poinsettias. In addition, Sulfotepp is recommended specifically for use on rose, stock, snapdragon, orchids, hydrangea, geranium, gardenia, foliage plants, cyclamen, chrysanthemum, carnation and azalea in New Jersey. Sulfotepp is also recommended in a number of state floricultural pesticide guides for ornamentals in general. In California, one or two applications of Sulfotepp are also used per crop (three crops per year) on gerbera daisies and hibiscus. In Pennsylvania, Sulfotepp is used by some growers in the spring on bedding plants, primarily cinerarias and calceolarias as well as poinsettias later in the year and likely on some roses (U.S. EPA, 1997a). Sulfotepp is usually applied in the evening. After ventilation the next morning, following the Agency's Worker Protection Standard guidelines, unrestricted entry is allowed.

2. Residential Use Products

There are no currently registered homeowner products for Sulfotepp. However, current labels do *not* prohibit application in residential greenhouses by certified commercial applicators.

E. Handler Exposures and Risks

1. Handler Exposure Scenarios

EPA has determined there are potential exposures to handlers during usual use patterns associated with Sulfotepp. Based on the use patterns, two major occupational scenarios were identified: (1) opening and lighting of canisters, and (2) reentering fumigated greenhouse to open vents and dispose of canisters.

No guideline/good laboratory practices (GLP) acceptable chemical-specific handler exposure data have been submitted to the Agency. Available data in PHED (Pesticide Handlers Exposure Database) do not reflect the use patterns of Sulfotepp.

a. Estimating Dermal Exposure to Handlers

For handlers, dermal exposures are assumed to be small relative to the exposures and risks from inhalation. This assumption is based on the use pattern where potential dermal exposure is limited to possible contact with the Sulfotepp formulated product, that is: (1) while opening the canisters and inserting the sparkler, (2) through an accidental spill during lighting of a canister or retrieval of an unlit canister, and (3) during possible contact with residue on the outside of a spent canister. These dermal exposures are expected to be relatively infrequent and of relatively short duration in comparison with the estimated inhalation exposure time and the potentially high air concentrations of Sulfotepp during handling activities. Therefore, only inhalation exposure and risk were estimated for handlers.

b. Estimating Inhalation Exposure to Handlers

EPA assessed a range of possible air concentration levels to which handlers could be exposed. A 1980 study by Williams *et.al.* published in the American Industrial Hygiene Association Journal (AIHAJ), measured on-site real-time Sulfotepp air levels in a greenhouse being fumigated (Williams, *et.al.*, 1980). In this study, the air concentration approximately four hours after the start of fumigation and before opening the vents and aerating the greenhouse was 2.7 mg/m^3 (200 ppb). This level was selected to represent a reasonable level possibly encountered by handlers igniting the canisters or entering following fumigation to activate the ventilation system.

EPA estimated the maximum air concentration levels potentially encountered by handlers by assuming that during fumigation all of the active ingredient in the smoke canister enters the greenhouse air at the label application rate. This concentration can be calculated as follows:

$$\text{Air concentration}\left(\frac{\text{mg ai}}{\text{m3}}\right) = \text{Application rate}\left(\frac{\text{lb ai}}{\text{ft3}}\right) * \text{Conversion Factors}\left(\frac{\text{mg ai}}{\text{lb ai}} * \frac{\text{ft3}}{\text{m3}}\right)$$

The maximum potential air concentration is 52.5 mg ai/m^3 based on the label application rate.

c. Other Assumptions

The following assumptions were used to complete the handler exposure and risk assessment:

- Handlers are assumed to be exposed intermittently to Sulfotepp (e.g., up to one hour on the day of application; up to one hour on the following day for venting; then repeating the exposure for an application on day three). Therefore, short-term risks are assessed, but not intermediate-term or chronic risks.

- The exposure period for handlers would depend on the size and number of greenhouses and, therefore, how many canisters must be lit. EPA estimates that the exposure period would likely range from approximately ten minutes for smaller greenhouses to an hour for larger greenhouses. A single handler could treat multiple greenhouses per day, so this range may actually underestimate actual exposure duration.

- The same Sulfotepp air concentration is assumed to be encountered by handlers when they apply and light smoke canisters and when they enter the treated greenhouse to open vents and dispose of canisters. These two activities are considered as a single exposure scenario for purposes of this exposure assessment.

2. Handler Exposure and Non-Cancer Risk Estimates

a. Handler Inhalation Risk Estimates

The estimates of Sulfotepp air concentration to which handlers may be exposed are used to calculate the risk to those handlers. The route-specific inhalation MOE was calculated as follows:

$$MOE = \frac{NOEL(mg / m3) * DA * AFA}{Human\ Airborne\ Concentration\ (mg / m3) * DH * AFH}$$

where:

D_A Duration of daily exposure for test animals (hours/day)
D_H Duration of daily exposure for humans (hours/day)
AF_A Activity factor for test animals (default is one)
AF_H Activity factor for humans (accounts for activity-related variation in respiration)

The activity factor for humans is based on the assumption that handler activities are most similar to the category titled sedentary.

Table 2 provides estimated inhalation risks to handlers based on the above assumptions and formula at baseline (i.e., without the use of PPE) and with risk mitigation (i.e., with the use of various types of respirators).

Table 2. Occupational Handlers' Inhalation Risks from Sulfotepp

Level of Protection	Air Concentration (mg ai/m^3)[a]	Respirator Protection Factor[b]	Human Exposure Duration (hr/day)[c]	Human Activity Factor[d]	Animal Exposure Duration (hr/day)[e]	Animal Activity Factor[f]	Animal Inhalation NOEL (mg/m^3)[g]	Inhalation MOE[h] (0.5 hr/1 hr)
Baseline (no respirator)	52.5	1	0.5/1	1.3	6	1	1.9	0.3/0.2
	2.7	1	0.5/1	1.3	6	1	1.9	6/3
Half-face organic-vapor-removing respirator	52.5	10	0.5/1	1.3	6	1	1.9	3/2
	2.7	10	0.5/1	1.3	6	1	1.9	65/32
Full-face organic-vapor-removing respirator	52.5	50	0.5/1	1.3	6	1	1.9	17/8
	2.7	50	0.5/1	1.3	6	1	1.9	320/160

Level of Protection	Air Concentration (mg ai/m^3)[a]	Respirator Protection Factor[b]	Human Exposure Duration (hr/day)[c]	Human Activity Factor[d]	Animal Exposure Duration (hr/day)[e]	Animal Activity Factor[f]	Animal Inhalation NOEL (mg/m^3)[g]	Inhalation MOE[h] (0.5 hr/1 hr)
Self-contained breathing apparatus	52.5	10,000	0.5/1	1.3	6	1	1.9	3,300/1,700
	2.7	10,000	0.5/1	1.3	6	1	1.9	65,000/32,000

[a]Air concentration of 52.5 mg ai/m^3 is the maximum theoretical air concentration based on label application rate (EPA Reg. No. 8241-10). Preventilation air concentration of 2.7 mg ai/m^3 (approximately four hours following the start of fumigation) represents the air concentration encountered by handlers when they enter the greenhouse to ventilate following fumigation as reported in the *AIHAJ* study on site determination of Sulfotepp air levels in a fumigating greenhouse (Williams, *et.al*., 1980).

[b]Respirator protection factor is the theoretical reduction in the Sulfotepp concentration in air provided by respiratory protection worn by a handler from the NIOSH Guide to Industrial Respiratory Protection (NIOSH, 1987). Baseline (represents handlers wearing no respirator) is assigned a protection factor of one (no protection); Half-face organic-vapor-removing respirator is assigned a protection factor of ten. (90% protection); Full-face organic-vapor-removing respirator with a HEPA prefilter is assigned a protection factor of 50 (98% protection); Self-contained breathing apparatus is assigned a protection factor of 10,000 (99.99% protection).

[c]Human exposure duration is based on the estimate of handler exposures of 30 minutes to one hour.

[d]Human activity value based on assumption that handler activities are equivalent to sedentary activities. Based on activity-specific inhalation rates listed in EPA's "Exposure Factors Handbook" (U.S. EPA, 1997b).

[e]Animal exposure duration of six hours per day is the daily exposure duration the test animals were subjected to in the study from which the inhalation endpoint is taken.

[f]Animal activity factor of one is based on the assumption that the test animals were at rest during the exposure study from which the inhalation endpoint is taken.

[g]Animal inhalation NOEL is 1.9 mg/m^3 in the animal inhalation exposure study (Kimmerle, *et.al*., 1974).

[h]MOE = [(animal inhalation NOEL) x (animal exposure duration) x (animal activity factor)]/[(air concentration) x (human exposure duration) x (human activity factor) x (respiratory protection factor)]

b. Handler Exposure and Cancer Risk Estimates

No carcinogenicity studies have been required or reviewed by the Agency.

c. Summary of Risk Concerns for Handlers, Data Gaps, and Confidence in Exposure and Risk Estimates

i. Risk Concerns for Handlers

Table 2 presents estimates of occupational handlers' inhalation risks from Sulfotepp. Due to the lack of acceptable data for Sulfotepp, HED has not determined an MOE that is considered adequate. Results indicate:

- With no respirator (baseline) the MOEs are less than 10; the highest MOE is six.

- With a half-face organic vapor-removing respirator with a dust/mist prefilter, the highest MOE is 65.

- With the full-face organic vapor-removing respirator with a HEPA prefilter, the highest MOEs is 17 at the 52.5 mg ai/m^3 air concentration level. The MOE is 320 at the 2.7 mg ai/m^3 level.

- With the self-contained breathing apparatus, MOEs exceed 1700.

ii. Data Quality and Confidence in Assessment

The risk estimate for handlers is based on several assumptions that reflect on the confidence of this assessment:

- If no PPE (e.g., gloves, double-layer body protection) is worn, dermal exposure may be greater than assumed since there are opportunities for dermal contact with Sulfotepp during the lighting of the canisters (e.g., puncturing the canisters, inserting the sparkler, spilling) and during removal of the canisters following application (e.g., residue on canister, spilling contents of unlit canister).

- The toxicological database is inadequate. The inhalation endpoint (NOEL of 1.9 mg/m^3) is derived from data generated in 1974 that was used to

established the TLV and PEL, but the data do not meet EPA guidelines or GLP requirements.

- The duration of exposure is based on the best professional judgement. No actual data are available.

- The air concentration levels are estimates of possible exposures. One is the maximum theoretical air concentration (vapor and particulate) based on the labeled application rates. The other air concentration level was taken from a 1980 *AIHAJ* study and was a measurement of Sulfotepp air concentration conducted approximately four hours following the start of fumigation but prior to aerating the greenhouse. The study does not meet EPA guidelines or GLP requirements.

- EPA has concerns about whether the *AIHAJ* study was conducted in conformity with current Sulfotepp labeling directions and has uncertainties about study conditions.

  -- In the *AIHAJ* study, 22 grams of Sulfotepp formulated product were used to fumigate a greenhouse with a volume of 450 m^3, which is equivalent to a rate of 0.048 g ai/m^3. The current Sulfotepp label rate is 0.0525 g ai/m^3 (seven ounces of formulated product per 20,000 cubic feet).

  -- In the *AIHAJ* study, the door was sealed and entry was prohibited after fumigation. Reentry was allowed to partially open vents and remove canisters four hours after ignition of the fumigant. There were no internal fans operating in the greenhouse and dissipation of Sulfotepp was by convection and diffusion only. Currently one Sulfotepp product label (Plantfume 103) directs users to "close all greenhouse vents prior to use," and "maintain treatment conditions overnight," or "open ventilators 2 to 3 hours after fumigation on

tender plants." The other Sulfotepp product label (Fulex Dithio Smoke) directs users to "close all greenhouse vents prior to use," "it is advisable to ventilate the greenhouse within twelve hours from the start of treatment -- ventilation at the end of eight hours is more desirable if possible."

-- In the *AIHAJ* study, the relative humidity ranged from 40 to 60 percent (not controlled) and temperature was maintained at 21°C during the day and 10°C during the night (11 p.m. to 7 a.m.). Both Sulfotepp product labels indicate that the relative humidity should be kept low and that temperatures within the greenhouse should be maintained between 70°F and 90°F (21°C to 32°C).

-- In the *AIHAJ* study, the number and the size of vents were not specified, which would have had effects on the dissipation of Sulfotepp residues. Also the time at which the vents were opened and the number of vents opened was not specified.

F. Postapplication Exposures And Risks

1. Postapplication Exposure Scenarios

EPA has determined there are potential postapplication dermal and inhalation exposures to workers during usual work practices following applications of Sulfotepp. Two major occupational scenarios were identified: (1) entry to perform watering or other routine low-exposure tasks; and (2) entry to perform harvesting, transferring, or other high-exposure tasks. Since one of the primary uses is just before marketing to ensure the pest-free status of plants, EPA assumes routine entry to perform hand labor tasks, such as watering, tending, harvesting, and preparing plants for shipment, would be initiated as soon as possible, normally the morning following an evening application. EPA notes that label instructions and other use information indicate that applications may be repeated every three days until the plants are free of pests. In practice, two to three applications at three-day intervals is usual and workers might be expected to have daily exposures for more than a week, depending on how

rapidly Sulfotepp dissipates. Therefore, intermediate-term as well as short-term risks should be assessed.

No guideline/GLP acceptable Sulfotepp-specific postapplication exposure data were submitted or reviewed by EPA in support of the reregistration of Sulfotepp.

a. Estimating Dermal Exposure to Postapplication Workers

Data reported in a 1986 degradation study conducted by the California Department of Food and Agriculture (CDFA) were used for estimating Sulfotepp postapplication dermal exposures and risks (CDFA, 1987). The CDFA study reported dislodgeable foliar residue (DFR) values for Sulfotepp on poinsettias at two sites and on geraniums at one site. DFR data for the poinsettias at site two were chosen as representative DFRs for the dermal exposure assessment. DFR values for poinsettias at site one were slightly lower and DFR values for geraniums at site three were slightly higher. Similar DFR values were found in a 1978 study published in the Journal of Environmental Science and Health that measured "likely to collect on the upper surfaces of exposed leaves." (Williams, 1978). The average surface concentration measured in that study 24 hours after the start of the fumigation (0.021 $\mu g/cm^3$) is similar to the DFR measured at 24 hours in the CDFA study (0.02 $\mu g/cm^3$). Neither study meets current U.S. EPA guidelines or GLP criteria (U.S. EPA, 1996).

In lieu of Sulfotepp-specific data on transfer coefficients, a default transfer coefficient of 1,000 was used to represent low dermal exposure activities (tending and watering) and 10,000 was used to represent relatively high dermal exposure activities (harvesting and preparing for shipping).

b. Estimating Inhalation Exposure to Postapplication Workers

EPA assessed a range of possible air concentration levels to which postapplication workers could be exposed. A 1980 study by Williams *et.al.* published in *AIHAJ* measured on-site real-time Sulfotepp air levels in a fumigated greenhouse. In this study, the air concentration was measured starting approximately four hours after the start of fumigation and before opening the vents to aerate the greenhouse, continuing until approximately 48 hours following the start of fumigation (Williams, *et.al*., 1980). EPA selected a range of air concentration levels that were

measured from the time initial post-fumigation ventilation was complete and continuing through the 48 hour period. The highest post-ventilation air concentration level was 0.34 mg ai/m^3 (25 ppb), the lowest steady post-ventilation level was 0.040 mg ai/m^3 (3 ppb), and a reelevated post-ventilation level (an increased air concentration level apparently caused by watering the plants) was 0.15 mg ai/m^3 (11 ppb). The *AIHAJ* study also measured Sulfotepp air concentration levels 18 days following application to be 0.0013 mg ai/m^3 (0.097 ppb). EPA used this level as a baseline air concentration level.

c. Other Assumptions

The following assumptions were used to complete the postapplication exposure and risk assessment:

- Postapplication workers are assumed to be exposed continuously to Sulfotepp (e.g., eight hours per day for a week or more), particularly when application is repeated every three days for two to three applications. Therefore, short- and intermediate-term risks are assessed.

- Average postapplication work period is eight hours per day.

- Average body weight is 70 kg for an adult handler.

- One hundred percent dermal absorption was used.

2. Postapplication Exposure and Non-Cancer Risk Estimates

a. Postapplication Dermal Risk Estimates

The calculations of postapplication daily dermal exposures to Sulfotepp were used to calculate the daily doses, and hence the risks, to workers reentering the fumigated greenhouse. Potential daily dermal exposure was calculated using the following formula:

$$\text{Daily Dermal Exposure } \left(\frac{mgai}{day}\right) =$$

$$\text{DFR } \left(\frac{ugai}{cm2}\right) \times \text{TransferCoefficient } \left(\frac{cm2}{hour}\right) \times 0.001 \frac{mg}{ug} \times \text{ExposureDuration } \left(\frac{hours}{day}\right)$$

The potential daily dermal dose was calculated using a 70 kg body weight as follows:

$$\text{Daily Dermal Dose}\left(\frac{\text{mg ai}}{\text{kg/day}}\right) = \text{Daily Dermal Exposure}\left(\frac{\text{mg ai}}{\text{day}}\right) x \left(\frac{1}{\text{Body Weight (kg)}}\right)$$

The short-term MOE was calculated using the estimated NOEL value of (0.14 mg ai/kg/day) and the intermediate-term MOE was calculated using the NOEL value (0.014 mg ai/kg/day). The following formula describes the calculation of the MOE:

$$MOE = \frac{NOEL\left(\frac{\text{mg ai}}{\text{kg/day}}\right)}{\text{Daily Dermal Dose}\left(\frac{\text{mg ai}}{\text{kg/day}}\right)}$$

Table 3 provides estimated short- and intermediate-term exposures and risks to postapplication workers.

Table 3. Postapplication Dermal Exposures and Risks to Occupational Workers from Sulfotepp

Exposure Scenario	Dislodgeable Foliar Residues (µg ai/cm^2)[a]	Transfer Coefficient (cm^2/hr)[b]	Exposure Duration (hr/day)[c]	Daily Dermal Exposure (mg ai/day)[d]	Daily Dermal Dose (mg ai/kg/day)[e]	Short-Term MOE[f]	Intermediate-Term MOE[g]
Low Exposure Activity (tending)	0.04 (15 hr after fumigation)	1000	8	0.32	0.0046	30	3
	0.02 (24 hr after fumigation)	1000	8	0.16	0.0023	61	6
	0.01 (38 hr after fumigation)	1000	8	0.08	0.0011	120	12
High Exposure Activity (harvesting, preparing for shipping)	0.04 (15 hr after fumigation)	10000	8	3.2	0.046	3	0.3
	0.02 (24 hr after fumigation)	10000	8	1.6	0.023	6	0.6
	0.01 (38 hr after fumigation)	10000	8	0.8	0.011	12	1.2

[a]Based on the DFR data from *A Study to Establish Degradation Profiles for Six Pesticides (Triforine, Endosulfan, Chlorothalonil, Sulfotepp, Dodemorph Acetate, and Daminozide) Used on Ornamental Foliage in San Diego County California During Fall 1986* (CDFA, 1987).

[b]Transfer coefficients of 1,000 and 10,000 cm^2/ hour were used to represent low and high exposure activities, respectively.

[c]Based on eight working hours per day.

[d]Daily dermal exposure (mg/day) = (Dislodgeable Foliar Residues (µg/cm^2)) x (Transfer coefficient (cm^2/hr)) x (0.001 mg/μg) x (Exposure duration (hr/day)).

[e]Daily dermal dose (mg/kg/day) = Daily dermal exposure (mg/day)/Body weight (70 kg).

[f]Short-term MOE = [(Short-term oral NOEL (0.14 mg/kg/day)) x (100% dermal absorption)/[daily dermal dose (mg/kg/day)].

[g]Intermediate-term MOE = [(Intermediate-term oral NOEL (0.014 mg/kg/day)) x (100% dermal absorption)]/[Daily dermal dose (mg/kg/day)].

b. Postapplication Inhalation Risk Estimates

The estimates of Sulfotepp air concentration to which postapplication workers may be exposed are used to calculate the risk to those workers. The route-specific inhalation MOE was calculated as follows:

$$MOE = \frac{NOEL(mg/m3) * D_A * AF_A}{Human\ Airborne\ Concentration\ (mg/m3) * D_H * AF_H}$$

where:

- **D_A** Duration of daily exposure for test animals (hours/day)
- **D_H** Duration of daily exposure for humans (hours/day)
- **AF_A** Activity factor for test animals (default is one)
- **AF_H** Activity factor for humans (accounts for activity-related variation in respiration)

The activity factor for humans is 2.2 for postapplication workers based on the assumption that an equal mix of light and moderate activities are performed (U.S. EPA, 1998c).

Table 4 provides estimated inhalation risks to postapplication workers based on the above assumptions, the range of post-ventilation air concentration levels, and the formula.

Table 4. Postapplication Inhalation Risks to Occupational Workers from Sulfotepp

Inhalation Exposure Scenario	Air Concentration (mg ai/m^3)[a]	Human Exposure Duration (hr/day)[b]	Human Activity Factor[c]	Animal Exposure Duration (hr/day)[d]	Animal Activity Factor[e]	Animal Inhalation NOEL (mg/m^3)[f]	Inhalation MOE[g]
AIHAJ highest air concentration within 48 hours of fumigation and after initial ventilation	0.34 (25 ppb)	8	2.2	6	1	1.9	2
AIHAJ medium air concentration within 48 hours of fumigation and after initial ventilation (following watering)	0.15 (11 ppb)	8	2.2	6	1	1.9	4
AIHAJ lowest and steady air concentration within 48 hours of fumigation and after initial ventilation	0.040 (3 ppb)	8	2.2	6	1	1.9	16
AIHAJ baseline air concentration level (18 days after fumigation)	0.0013 (0.097 ppb)	8	2.2	6	1	1.9	500

[a]The air concentration ranges are based on results in the *AIHAJ* study *On site determination of Sulfotepp air levels in a fumigating greenhouse (*Williams, *et.al.,* 1980).

[b]Human exposure duration is based on the estimate of worker postapplication exposures of eight hours per day.

[c]Human activity value based on assumption that handler activities are equivalent to light work activities. Based on activity-specific inhalation rates listed in the "Exposures Factor Handbook "(U.S. EPA, 1997b).

[d]Animal exposure duration of six hours per day is the daily exposure duration the test animals were subjected to in the study from which the inhalation endpoint is taken.

[e]Animal activity factor of one is based on the assumption that the test animals were at rest during the exposure study from which the inhalation endpoint is taken.

[f]Animal inhalation NOEL is 1.9 mg/m^3 in the animal inhalation exposure study (Kimmerle, *et.al*., 1974).

[g]MOE = [(animal inhalation NOEL) x (animal exposure duration) x (animal activity factor)]/[(air concentration) x (human exposure duration) x (human activity factor)]

c. Postapplication Total Risk Estimates

Since both the dermal and inhalation risks to postapplication workers are based on the same toxicological endpoint of concern -- cholinesterase inhibition -- the estimated dermal and inhalation risks can be combined to obtain total estimated risk to workers. The total MOE was calculated using the following formula:

$$Total\ MOE = \frac{1}{\left(\frac{1}{MOE_{dermal}}\right) + \left(\frac{1}{MOE_{inhalation}}\right)}$$

The short-term total risk is calculated by adding the reciprocals of the short-term dermal MOE and the inhalation MOE and dividing the total into one. Intermediate-term total risk is calculated by adding the reciprocals of the intermediate-term dermal MOE and the inhalation MOE and dividing the total into one.

d. Postapplication Cancer Risk Estimates

No carcinogenicity studies for Sulfotepp were required or reviewed by the Agency.

e. Summary of Postapplication Risk Concerns, Data Gaps, and Confidence in Exposure and Risk Estimates

i. Postapplication Dermal Risk Concerns

Short- and intermediate-term dermal postapplication risk concerns are presented in Table 3. Due to the lack of acceptable data for Sulfotepp, HED has not determined an MOE that is considered adequate. Results indicate:

- Short-term dermal MOEs for *low exposure* activities are greater than 100 (MOE = 120) at 38 hours following fumigation. MOEs are less than 100 at both 15 hours and 24 hours following fumigation.

- Short-term dermal MOEs for *high exposure* activities are less than 100 at 15 hours, 24 hours, and 38 hours following fumigation.

- Intermediate-term dermal MOEs for *low exposure* activities are less than 100 at 15 hours, 24 hours, and 38 hours following fumigation.

- Intermediate-term dermal MOEs for *high exposure* activities are less than 100 at 15 hours, 24 hours, and 38 hours following fumigation.

ii. Postapplication Inhalation Risk Concerns

Inhalation postapplication risks are presented in Table 4. Due to the lack of acceptable data for Sulfotepp, HED has not determined an MOE that is considered adequate. Results indicate that inhalation MOEs are less than 100 (<20) for all air concentrations measured within 48 hours of fumigation and after initial ventilation. The MOE at baseline air concentration measured 18 days following application is greater than 100 (500).

iii. Postapplication Total Risk Concerns

Total postapplication risks are presented in Table 5. Due to the lack of acceptable data for Sulfotepp, HED has not determined an MOE that is considered adequate. Results indicate that:

- Total short-term MOEs are less than 100 (ranging from 1 to 14) at all air concentration levels for both low and high exposure activities up to 38 hours following fumigation.

- Total intermediate-term MOEs are less than 100 (ranging from 0.3 to seven) at all air concentration levels for both low and high exposure activities up to 38 hours following fumigation.

Table 5. Postapplication Total (Inhalation plus Dermal) Risks to Occupational Workers from Sulfotepp

Exposure Scenario[a]	Short-Term Dermal MOE[a]	Intermediate-Term Dermal MOE[a]	Inhalation MOE[b]	Total Short-Term MOE[c]	Total Intermediate-Term MOE[d]
Low Exposure Activity (tending)	30 (15 hr after fumigation)	3	2 (*AIHAJ* high)	2	1
			4 (*AIHAJ* medium)	4	2
			16 (*AIHAJ* low)	10	3
	61 (24 hr after fumigation)	6	2 (*AIHAJ* high)	2	2
			4 (*AIHAJ* medium)	4	2
			16 (*AIHAJ* low)	13	4
	120 (38 hr after fumigation)	12	2 (*AIHAJ* high)	2	2
			4 (*AIHAJ* medium)	4	3
			16 (*AIHAJ* low)	14	7
High Exposure Activity (harvesting, preparing for shipping)	3 (15 hr after fumigation)	0.3	2 (*AIHAJ* high)	1	0.3
			4 (*AIHAJ* medium)	2	0.3
			16 (*AIHAJ* low)	3	0.3
	6 (24 hr after fumigation)	0.6	2 (*AIHAJ* high)	2	0.5
			4 (*AIHAJ* medium)	2	0.5
			16 (*AIHAJ* low)	4	0.6
	12 (38 hr after fumigation)	1.2	2 (*AIHAJ* high)	2	0.8
			4 (*AIHAJ* medium)	3	1
			16 (*AIHAJ* low)	7	1

[a]Based on Table 3: Postapplication Dermal Exposures and Risks to Occupational Workers from Sulfotepp.

[b]Based on Table 4: Postapplication Inhalation Risks to Occupational Workers from Sulfotepp.

[c]Short-term Total MOE is calculated by adding the reciprocals of the short-term dermal MOE and the inhalation MOE and dividing the total into one.

[d]Intermediate-term Total MOE is calculated by adding the reciprocals of the intermediate-term dermal MOE and the inhalation MOE and dividing the total into one.

iv. Data Quality and Confidence in Assessment

The risk estimates for postapplication workers are based on several assumptions that reflect on the confidence of this assessment:

- Inhalation and dermal exposure and risk may be even higher after the second or third application due to accumulation of Sulfotepp in the greenhouse.

- A working period of eight hours per day was assumed, which might result in overestimation of the risks for some activities.

- For the dermal assessment:

  -- The short-term dermal NOEL is an *estimate* derived from an intermediate-term (13 week) NOEL from an oral study in dogs.

  -- Transfer coefficients of 1,000 and 10,000 for low and high exposure activities respectively were assumed; however, there were no data available that could verify the selection of these values.

  -- DFR values were obtained from a 1986 degradation study conducted by CDFA (CDFA, 1987). However, EPA review found the study to be unacceptable to fulfill the requirements for guideline 875.21 (DFR) and is not upgradeable to an acceptable study (U.S. EPA, 1996). It was not performed under GLP conditions and there was no GLP process imposed. In addition, factors that could have affected Sulfotepp residue levels were not documented in entirety in this study. Finally, CDFA indicated to EPA that the study should not be used to support any regulatory action and that California itself would not accept this study to support any type of regulatory action.

-- DFR values are available only for the first 38 hours following fumigation. These values result in MOEs less than 100. No DFR data are available to assess how long following fumigation when dermal exposures and risks would be greater than 100.

· For the inhalation assessment:

-- The endpoint (NOEL of 1.9 mg/m^3) is derived from data generated in 1974 that is not a guideline/GLP acceptable study.

-- The postapplication air concentration levels were taken from a 1980 *AIHAJ* study that is not a guideline/GLP acceptable study. EPA has concerns whether the *AIHAJ* study was conducted in conformity with current Sulfotepp labeling directions and has uncertainties about study conditions (see "Data Quality and Confidence in Assessment" in the handler exposure and risk assessment).

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